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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,002	03/30/2004	Balram Ghosh	206,487	6062

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,002	GHOSH ET AL.	
	Examiner	Art Unit	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *105-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on July 6, 2007 is acknowledged and has been entered. Claims 1-104 have been canceled. Claims 105-120 have been added. Claims 105-120 are pending.

Claims 105-120 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL.

Previous Rejections

The rejection of claims 1-19, 29 and 77-85 under 35 U.S.C. 101 is withdrawn in view of Applicant's cancellation of the claims. The rejections under 35 U.S.C. 112 and the objections to the claims are withdrawn in view of cancellation of the claims.

New Grounds of Rejection as necessitated by Applicant's amendment to the claims.

Claim Rejections - 35 USC § 112, 2nd paragraph

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 105-118 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Regarding claims 105-106, 109, 111, 113, 114, 117, the term 'R1 allelic variant' in the preamble is not clearly defined or specifically claimed. What structural limitation does this limitation impose on the claim?

4. Regarding claims 107-108, 110, 112, 115-116, the term 'R3 allelic variant' in the preamble is not clearly defined or specifically claimed. What structural limitation does this limitation impose on the claim?

5. Regarding claims 113-116, it is unclear from the claim how the "percentage frequency of the R1 locus dinucleotide" (claims 16-17) or the "percentage frequency of the R3 locus dinucleotide" (claims 18-19) imposes a structural limitation on the nucleic acid product represented by these claims?

Claim Interpretation

The term 'R1 allelic variant' and 'R3 allelic variant' are not clearly defined in the claims and instead are referred to as allelic variants. The R1 term is not explicitly defined, but is described as "The SEQ ID No. 1 has 1-392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 of R1 locus" (previous claim 1 and throughout specification, including paragraph 58 of PgPub). The R3 term is not explicitly defined, but is described as "the SEQ ID No.2 has 1 to 336 contiguous nucleotides containing

one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of R3 locus" (previous claim 1 and throughout specification, including paragraph 59 of PgPub). Therefore, the term R1 variant is being interpreted as reading on nucleotides 125-168 of SEQ ID NO:1 comprising a GT repeat region and the term R3 variant is being interpreted as reading on nucleotides 87-116 of SEQ ID NO:2 comprising a GT repeat region.

Claim Rejections - 35 USC § 102

6. Claims 105-108, 114-116 and 118-120 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al. (Genomics, 1998, vol. 52, p. 192-200). Patel teaches the mapping and characterization of the human STAT6 gene (Abstract).

With regard to claim 105, Patel teaches an isolated R1 allelic variant having SEQ ID NO: 1 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Patel or nucleotides 125-167 of SEQ ID NO:1 below),

```
Qy        121 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1028 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG1087
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With regard to claim 106 and 108, Patel teaches an isolated allelic variant according to claim 105, wherein the subject is human (see attached sequence alignment(s), where it is noted the sequence source is human).

With regard to claim 107, Patel teaches an isolated R3 alellic variant of SEQ ID NO: 2 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Patel or nucleotides 87-116 of SEQ ID NO:2 below).

```
Qy          61 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT 120
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        3665 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT

3724
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Regarding claims 114-116, the limitation directed to the percentage frequency of the specific R1 or R3 alleles does not place a structural limitation on the nucleic acid claimed. Therefore, these claims are considered rejected in view of the rejections stated previously above because the sequence of the R3 locus, or SEQ ID NO:2, depicts 15 repeats, meeting the limitation of claims 114-116.

With regard to claim 118, Patel teaches an isolated pharmacogenetic markers having SEQ ID NOS: 1 (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Patel or nucleotides 125-167 of SEQ ID NO:1 above) and 2 (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Patel or nucleotides 87-116 of SEQ ID NO:2 above) for detecting and predicting a predisposition to atopic asthma of STAT-6 gene in a subject.

With regard to claim 119, Patel teaches an isolated pharmacogenetic markers according to claim 118, wherein SEQ ID NO. 1 is associated with R1 locus (see attached sequence

alignment, HSSTATSIX1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Patel or nucleotides nucleotides 125-167 of SEQ ID NO:1 above) and SEQ ID No. 2 is associated with R3 locus of STAT-6 gene (see attached sequence alignment, HSSTATSIX1, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Patel or nucleotides 87-116 of SEQ ID NO:2 above).

With regard to claim 120, Patel teaches an isolated pharmacogenetic markers according to claim 118, wherein a subject is human (see attached sequence alignment(s), where it is noted the sequence source is human).

7. Claims 105-120 are rejected under 35 U.S.C. 102(a) as being anticipated by Nagarkatti et al. (Journal of Human Genetics, 2002, vol. 47, p. 684-687). Nagarkatti teaches the identification of three polymorphic (CA) repeat regions and the examination of allelic frequency and haplotypes was conducted (Abstract).

With regard to claim 105, Nagarkatti teaches an isolated R1 allelic variant having SEQ ID NO: 1 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951 referenced p. 685, col. 1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Nagarkatti or nucleotides 125-168 of SEQ ID NO:1 below; also see Table 1, 'STAT6 gene' heading)

```
Qy        121 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db       1028 AATCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGACGGAGTCTTG
1087.
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With regard to claim 106 and 108, Nagarkatti teaches an isolated allelic variant according to claim 105, wherein the subject is human (see p. 684-5, 'subjects and methods' where the individuals analyzed are described in detail; also see accession number AH006951, where it is noted the sequence source is human).

With regard to claim 107, Nagarkatti teaches an isolated R3 alellic variant of SEQ ID NO: 2 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene for use in predicting susceptibility of a subject to atopic asthma (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Nagarkatti or nucleotides 87-116 of SEQ ID NO:2 below; also see Table 1, 'STAT6 gene' heading).

```
Qy         61 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3665 CACTGAAGAGGGAGGACGGGAGAGGAGTGTGTGTGTGTGTGTGTGTGTGTGTATGT
3724
```

Regarding claims 109-112 and 117, while the inclusion of specific haplotypes imposes a structural limit on the number of CA repeats present in the sequence comprising SEQ ID NO:1 and 2, the limitations regarding specific p values does not impose a structural limitation on the nucleic acid sequence. Therefore, the claims are rejected solely on the basis of specific haplotypes disclosed by Nagarkatti.

With regard to claim 109-110, Nagarkatti teaches an isolated allelic variant according to claim 105 or 107, wherein CA nucleotide repeat is on 17 allele of R1 locus and on 15 allele of

R3 locus of the STAT-6 gene having a 'p' value less than 0.0031 and are associated with asthma (Table 2, where haplotypes comprising 17_15 were identified in the STAT-6 gene).

With regard to claim 111-112, Nagarkatti teaches an isolated allelic variant according to claim 105 or 107, wherein CA nucleotide repeat is on 16 allele of R1 locus and on 15 allele of R3 locus of the STAT-6 gene having a 'p' value less than 0.001 and are associated with asthma (Table 2, where haplotypes comprising 16_15 were identified in the STAT-6 gene).

With regard to claim 117, Nagarkatti teaches an isolated allelic variant according to claim 105, wherein haploypes 17__14 (CA repeat 17 in R1 locus and 14 in R3 locus of the STAT-6 gene having a 'p' value less than 0.00001), 23__16 (CA repeat 23 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24 16 (CA repeat 24 in R1 locus and 16 in R3 locus of the STAT-6 gene having a 'p' value less than 0.0001) are associated with protection from asthma (Table 2, where haplotypes 24_16 were identified in the STAT-6 gene; see also p. 686, col. 1, where it is noted that Table 2 represents 76% of all haplotypes and others were not included).

Regarding claims 113-116, the limitation directed to the percentage frequency of the specific R1 or R3 alleles does not place a structural limitation on the nucleic acid claimed. Therefore, these claims are considered rejected in view of the rejections stated previously above.

With regard to claim 118, Nagarkatti teaches an isolated pharmacogenetic markers having SEQ ID NOS: 1 (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951 referenced p. 685, col. 1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Nagarkatti or nucleotides 125-168 of SEQ ID NO:1 above; also see Table 1, 'STAT6 gene'

heading) and 2 (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Nagarkatti or nucleotides 87-116 of SEQ ID NO:2 above; also see Table 1, 'STAT6 gene' heading) for detecting and predicting a predisposition to atopic asthma of STAT-6 gene in a subject.

With regard to claim 119, Nagarkatti teaches an isolated pharmacogenetic markers according to claim 118, wherein SEQ ID NO. 1 is associated with R1 locus (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951 referenced p. 685, col. 1, specifically nucleotides 908-1299, which comprises SEQ ID NO:1 and the repeat region R1, located at nucleotides 1032-1074 of Nagarkatti or nucleotides 125-168 of SEQ ID NO:1 above; also see Table 1, 'STAT6 gene' heading) and SEQ ID No. 2 is associated with R3 locus of STAT-6 gene (see attached sequence alignment, HSSTATSIX1, which matches accession number AH006951, specifically nucleotides 3605-3940, which comprises SEQ ID NO:2 and the repeat region R3, located at nucleotides 3691-3720 of Nagarkatti or nucleotides 87-116 of SEQ ID NO:2 above; also see Table 1, 'STAT6 gene' heading).

With regard to claim 120, Nagarkatti teaches an isolated pharmacogenetic markers according to claim 118, wherein a subject is human (see p. 684-5, 'subjects and methods' where the individuals analyzed are described in detail; also see accession number AH006951, where it is noted the sequence source is human).

Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Nyce et al. (WO0062736; October 2000) discloses oligonucleotide compositions for prophylactic, preventive and therapeutic treatments associated with impaired respiration, lung allergies and/or inflammation and discloses sequences of STAT6 (Abstract and attached alignments).

Response to Arguments

8. Applicant's arguments filed July 6, 2007 have been fully considered but they are not persuasive.

Applicant traverses the rejection of the claimed subject matter under Patel. Applicant asserts "The Patel et al. reference does not report the repeats R1 and R3 and their alleles as claimed in the present invention. The Patel et al. reference also does not disclose or teach anything about asthma." Applicant also asserts "The Patel reference discloses the exon sequence of the STAT-6 gene, while the claimed invention is related to the upstream sequence of the STAT-6 repeat polymorphism and their haplotypes which are not even disclosed in the Patel et al. reference. (The Patel reference does not disclose SEQ ID NO 1 R1). The flanking sequences (upstream and downstream of TG repeat of R1 and its alleles) of the claimed invention (SEQ ID NO 1) are totally different and distinguishable from the disclosed flanking region of the STAT-6 gene of Patel" (page 6 of remarks).

Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of

the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

Next, the arguments that the sequence flanking the exonic sequence of SEQ ID NO:1 are different in Patel as compared to the claimed invention argues a feature that is not claimed, as there is no mention of flanking versus exonic sequence in the allelic variants as presently claimed. Furthermore, as Applicant has not clearly stated how the sequence of Patel distinguishes over the sequences of SEQ ID NO:1 or 2 or regarding the different flanking sequences the rejection is maintained. As stated in the art rejection above, Patel teaches the sequence of SEQ ID NO:1 and 2 and is interpreted as including the R1 and R3 repeats which are part of SEQ ID NO:1 and 2 respectively (see claim interpretation above).

It is also noted that the R1 and R3 loci features present in the preamble to the claim are not distinctly claimed in the new versions of the claims. In the previous slate of claims, the R1 locus was described as ""The SEQ ID No. 1 has 1-392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 of R1 locus" (previous claim 1 and throughout specification, including paragraph 58 of PgPub) and the R3 locus was described as "the SEQ ID No.2 has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of R3 locus" (previous claim 1 and throughout specification, including paragraph 59 of PgPub). It is under this interpretation based on the previous version of the claims and the teaching of the spec that both R1 and R3 are present in SEQ ID NO:1 and SEQ ID NO:2 that art rejections are applied.

In response to applicant's argument that Patel does not disclose or teach anything about asthma (referring to the use of the allelic variants in predicting susceptibility to disease), a

recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Furthermore, regarding the lack of specific teaching that the sequences are useful in diagnosing asthma, as noted in the previous art rejection, "the limitation regarding which disease that is associated with the specific gene variant does not impose a structural limitation on the sequence or structure of the nucleic acid. Therefore, these claims are rejected in view of the nucleic acid sequence, represented by AH006951 described above with regard to claims 1 and 2". The rejection is maintained.

Applicant traverses the rejection of the claimed subject matter as being anticipated by Nagarkatti. Applicant asserts "Quite simply, independent claims 105 and 118, and the claims dependent therefrom, are not disclosed by the Nagarkatti et al. reference. Since the claims distinguish over the reference, the 102(a) rejection has been overcome" (p. 7 of remarks).

Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections. Therefore, absent a specific teaching of how the Nagarkatti reference does not disclose the invention of independent claims 105 and 118, the rejection is maintained for the reasons stated in the art rejection above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephanie K. Mummert

Stephanie K Mummert, Ph.D.
Examiner
Art Unit 1637

SKM

JEFFREY FREDMAN
PRIMARY EXAMINER
9/19/07